Endocrine & Genitourinary Module
Biochemical basis Obesity & weight regulation

ILOs:

By the end of this lecture, you will be able to:

1. Interpret the biochemical basis of body weight regulation
2. Enumerate the causes of obesity
3. Outline effect of obesity

Case scenario

A 49 –year- old married woman, 158 cm tall and weighting 108 Kg came for consultation to a physician complaining of increased weight. She was too worried about her weight gain.

· She has sedentary life style. Her dietary habits revealed high caloric diet and absent consumption of vegetables and fruits
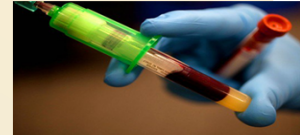
During routine physical examination:

the patient was observed to be hypertensive (blood pressure of 200/120 mm Hg).

- The patient was asked to return to the clinic during fasting state and blood specimen was obtained.

- **Lab investigation revealed:**

Parameter	level	Normal range
Blood glucose fasting	170 mg/dl	70-110 mg/dl
Insulin	50 mIU/L	< 25 mIU/L
Total cholesterol	280 mg/dl	120-220 mg/dl
Triglycerides	177 mg/dl	< 150mg/dl

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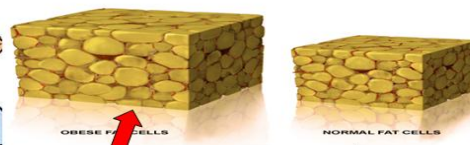
What is the most likely diagnosis?

Obesity.

What is Obesity?

Definition:

Obesity is a disorder of body weight regulatory systems characterized by an accumulation of excess body fat (increase fat cells size and number) either generalized or localized.
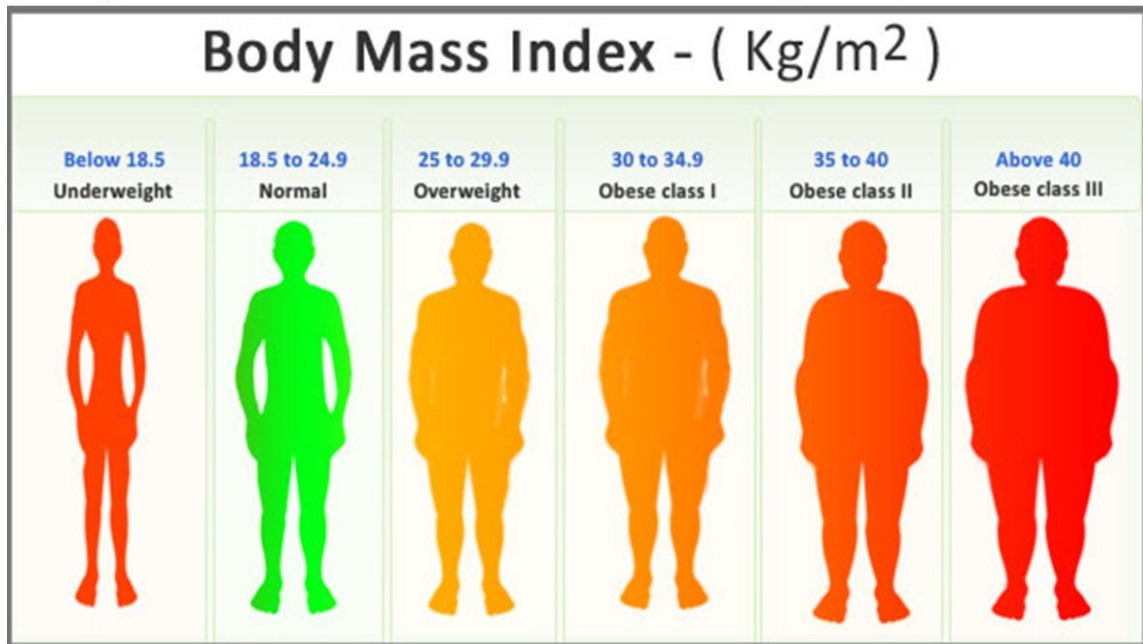
Expansion of fat cells

WHO classified the weight according to body mass index (BMI) into:

Body Mass Index - (Kg/m²)

Below 18.5 Underweight	18.5 to 24.9 Normal	25 to 29.9 Overweight	30 to 34.9 Obese class I	35 to 40 Obese class II	Above 40 Obese class III

Regulation of body weight

Long term signals (Hormones)

short term signals (minutes to hours)

1- Leptin (satiety hormone)
2- Insulin

1-GIT hormones
- Hunger: Ghrelin
- After meal: CCK,PYY
2-Neural signals
3-Hypothalamus

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1- Leptin (satiety hormone):

➢ Leptin is a hormone secreted mainly from **white adipose tissue**.

➢ Can be produced in very small amount by placenta, skeletal muscle, stomach ,liver, bone marrow, and mammary glands.

- Eating (meal) ⟶ stimulate leptin secretion

• **Blood level:**

Leptin **varies with fat mass**

Increased fat mass ⟶ increased leptin secretion.
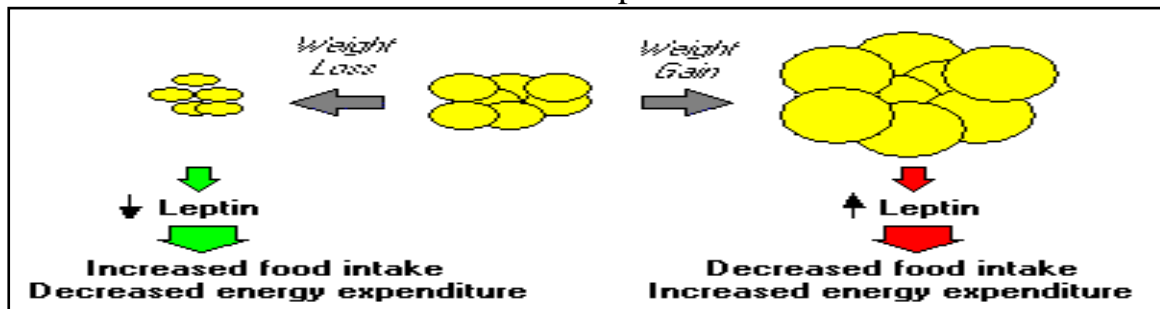
- **Function:**
    - Increase energy expenditure (loss)
    - It **considered a satiety hormone through:**

➢ **Directly**:

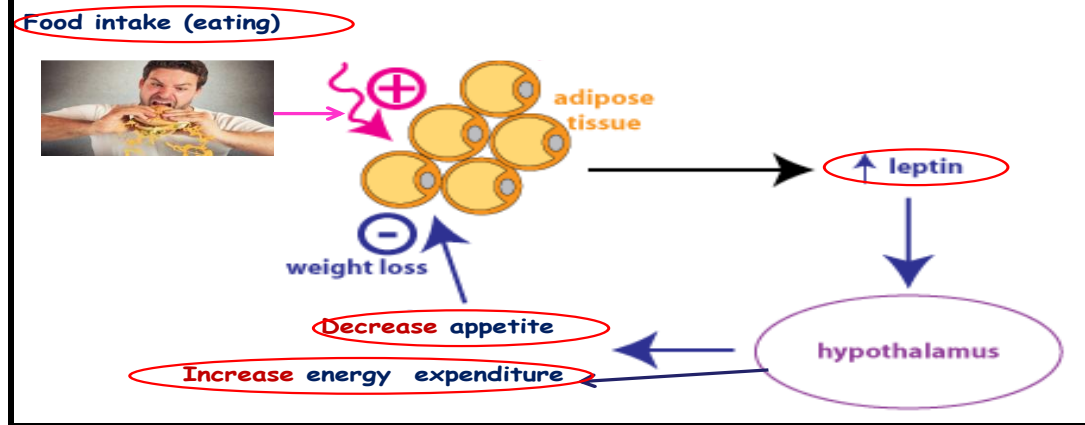Stimulate satiety center ⟶ (stop eating & Decrease appetite).

➢ **Indirectly:**
   I. Leptin can increase the sensitivity of hypothalamic satiety center to CCK ⟶ satiety
   II. Leptin can decrease the sensitivity of hypothalamic hunger center ⟶ no hunger sensation

1- Leptin (satiety hormone)

Food intake (eating)

adipose tissue

↑ leptin

weight loss

Decrease appetite

Increase energy expenditure

hypothalamus

What about Leptin levels in obesity?
Why leptin levels increased in obese person?

It is **increased** due to **increased body fat mass** in obese person**;** but there is **resistance to this leptin**.
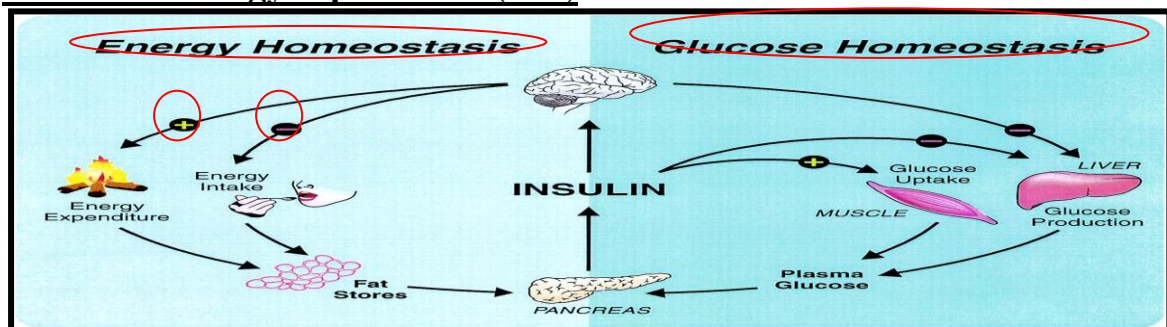
2- Insulin:
Insulin hormone secreted by β cells of pancreas
- A meal (eating): ↑blood glucose level ⟶ stimulate insulin secretion which leads to:

1-Decrease food intake :
Through increased sensitivity of satiety center to satiety signals ⟶ feel of satiety ⟶ stop eating.

2-Increase energy expenditure (loss)

Energy Homeostasis   Glucose Homeostasis

Energy Intake

INSULIN

Glucose Uptake

LIVER

Energy Expenditure

MUSCLE

Glucose Production

Fat Stores

Plasma Glucose

PANCREAS

B. **Short-term signals (minutes to hours)**

➢ Short-term signals from the gastrointestinal tract control hunger and satiety.

➢ They affect the size and number of meals
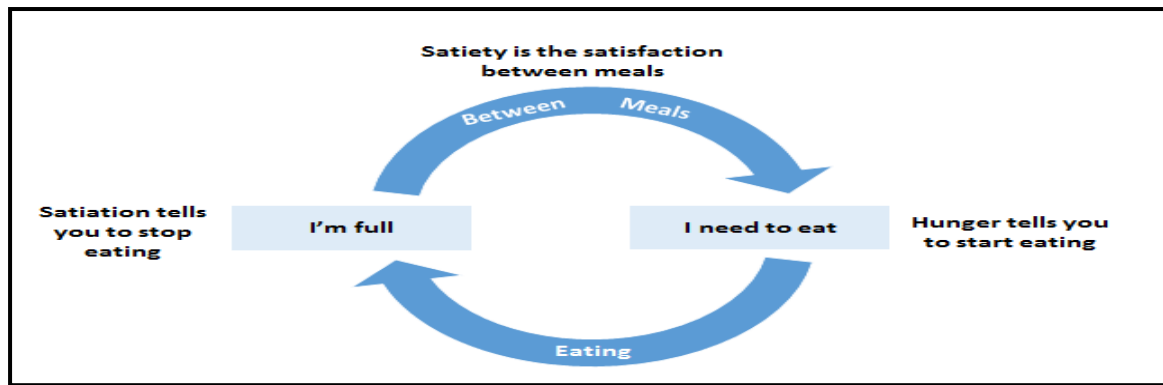
1-GIT hormones:

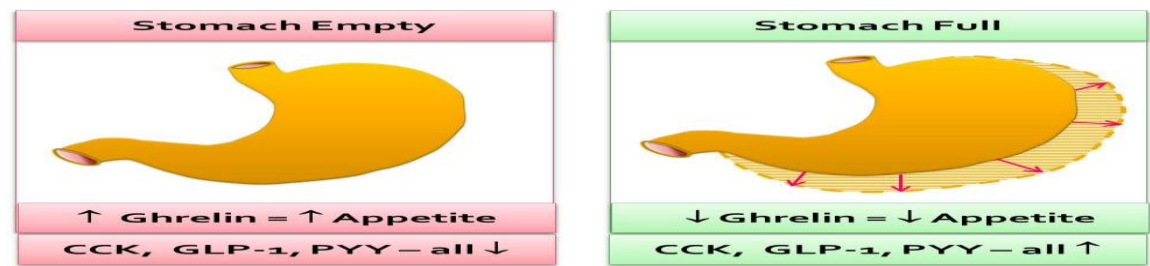**A)In the absence of food intake (between meals)**

1. **Ghrelin (appetite-stimulating) "hunger hormone"**

Source:

Produced by ghrelinergic cells in the gastrointestinal tract.

- **Function**

Hormone that stimulate hunger sensation.

B) After meal:

2-Cholecystokinin (CCK):

➤ **Cholecystokinin (CCK from Greek *chole*, "bile"; *cysto*, "sac"; *kinin*, "move".**

➤ **Source:**

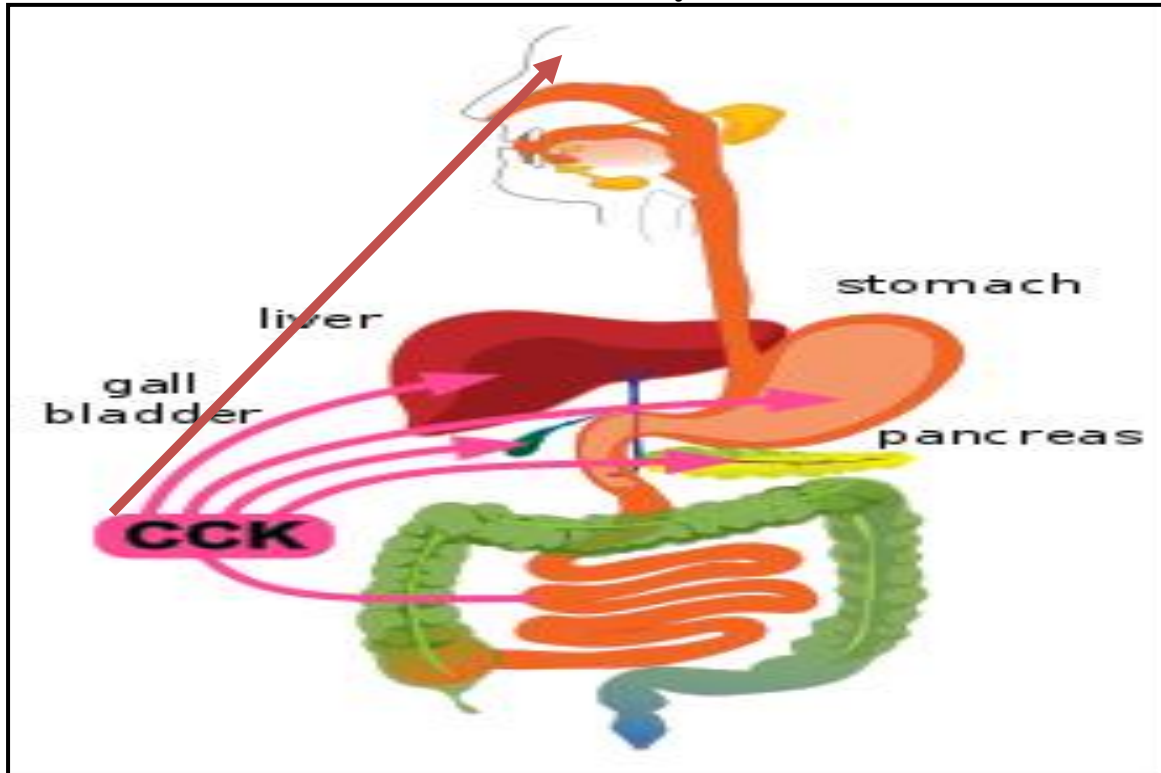 Is synthesized by enteroendocrine cells in the duodenum.

➤ It is released rapidly into circulation in response to a meal.

➤ **Function:**

• Inhibiting of feeding center (stop eating)

• Delay gastric emptying   give chance for digestion

• Contraction of gall bladder   release of bile which help in digestion

• Stimulate release of pancreatic enzyme in the small intestine.

2-Peptide YY (PYY):

> **Source:**

It is a peptide released from ileum and colon in response to feeding.

> **Action :**

- Inhibiting of feeding center

- Delay gastric emptying ⟶ give chance for digestion

2-Neural signals

- **Mechanical:**

Stomach felling by food (stretch) ⟶ neural signals transmitted by vagi nerves to the hypothalamus cause:

Stimulation of satiety center

Inhibition of feeding center ⟶ stop eating

3-Hypothalamus

The hypothalamus secrete neuropeptides such as:

i.   Hormone:

Alpha melanocyte stimulating hormone (α-MSH): inhibit

───────────────────────▶ feeding   satiety   sensation

ii.   Neurotransmitters:

Such as serotonin and dopamine are important in regulating hunger and satiety.

Adipose tissue as endocrine organ

Adipose tissue is now known to play an active role in body weight regulatory systems.

Adipose tissue is an endocrine cell that secretes a number of adipocytokine which act as hormones such as:

1-Leptin "satiety hormone"   2-Adiponectin

2-Adiponectin

- **Site of synthesis:**

Produced in mainly from adipose tissue.

- **Function**

- Reduces levels of blood free fatty acids.

- Improved lipid profile ──────→ Increase HDL cholesterol

  Decrease LDL cholesterol

  Decrease triglycerides

- Increase insulin sensitivity ──────→ better glycemic control

- Anti-inflammatory ──────→ Reduce inflammation

Causes of obesity

1-Lack of energy balance :

A lack of energy balance most often causes overweight and obesity . Energy balance means that energy IN equals energy OUT .

2-An inactive sedentary life

energy expenditure through metabolism and physical activity

energy intake from food and drink
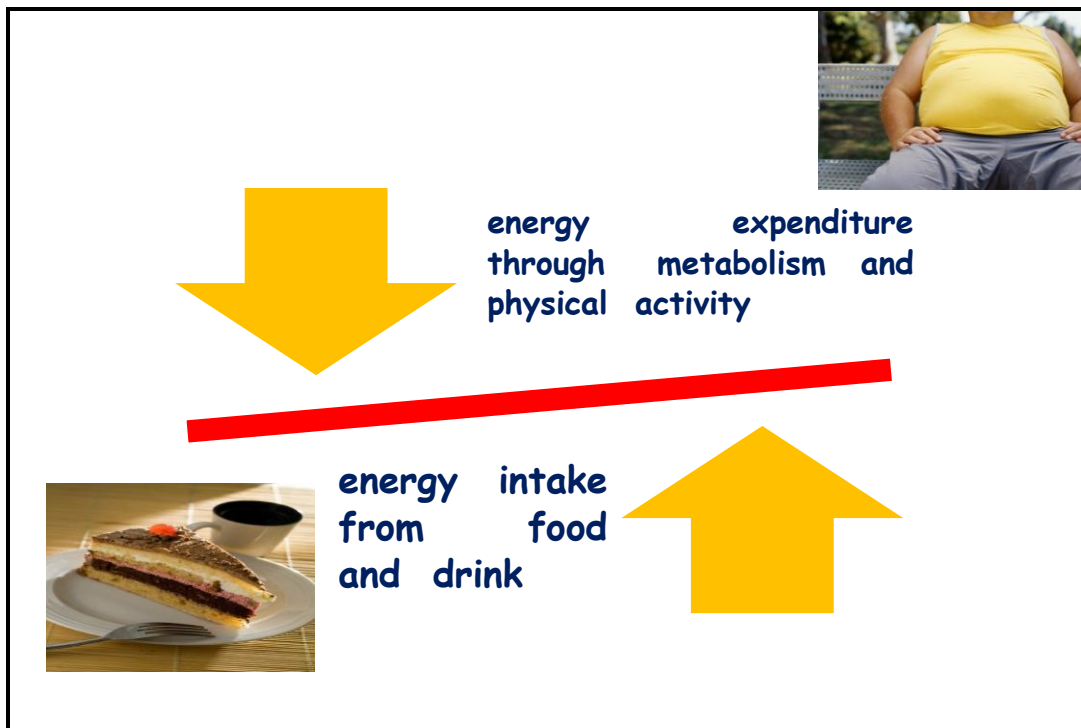
3-Environmental factors :

➢ Lack of sidewalk

➢ Oversized food portions

➢ fast foods

➢ Decreased consumption of healthy foods

4-Genes and family history:

Obesity has genetic basis??

➢ Identical twins have very similar body mass index (BMI) than those of non identical twins.

➢ **Gene Mutations :**

For example: some genetic mutation associated with :

▪ Hyperphagia

▪ Massive obesity

5-Hormonal disturbances :

➢ Hypothyroidism

➢ Cushing syndrome

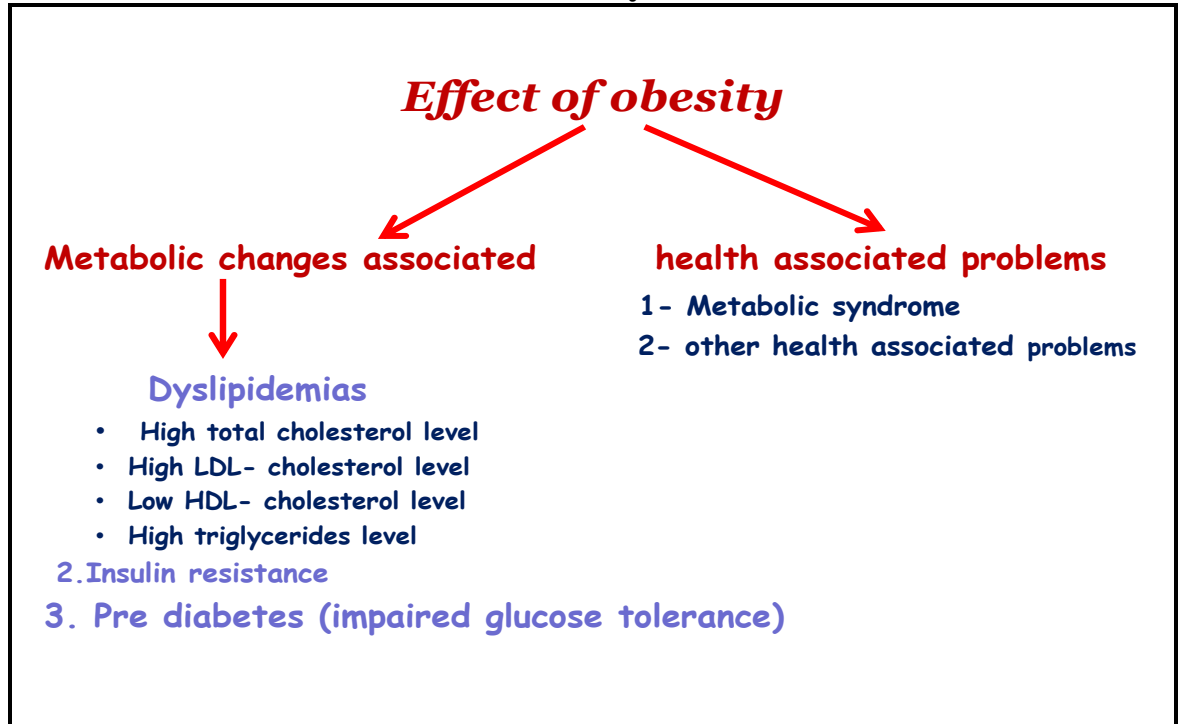➢ Polycystic ovarian syndrome .

6-Medicines :

➢ Corticosteroids

➢ Antidepressant

➢ Antiepileptic

7-Emotional factors:

Some people eat more than usual when they are bored, angry or stressed.

Effect of obesity

Metabolic changes associated   **health associated problems**

1- Metabolic syndrome
2- other health associated problems

Dyslipidemias
- High total cholesterol level
- High LDL- cholesterol level
- Low HDL- cholesterol level
- High triglycerides level

2. Insulin resistance

3. Pre diabetes (impaired glucose tolerance)

What health problems associated with obesity?

Obesity leads to increased risk of developing associated diseases, such as:

- Arthritis.   . Diabetes

- Metabolic syndrome   . Athersclerosis

- Hypertension,

- Cardiovascular disease

- Cancer.

- Fatty liver.

- Depression

- Gallbladder diseases
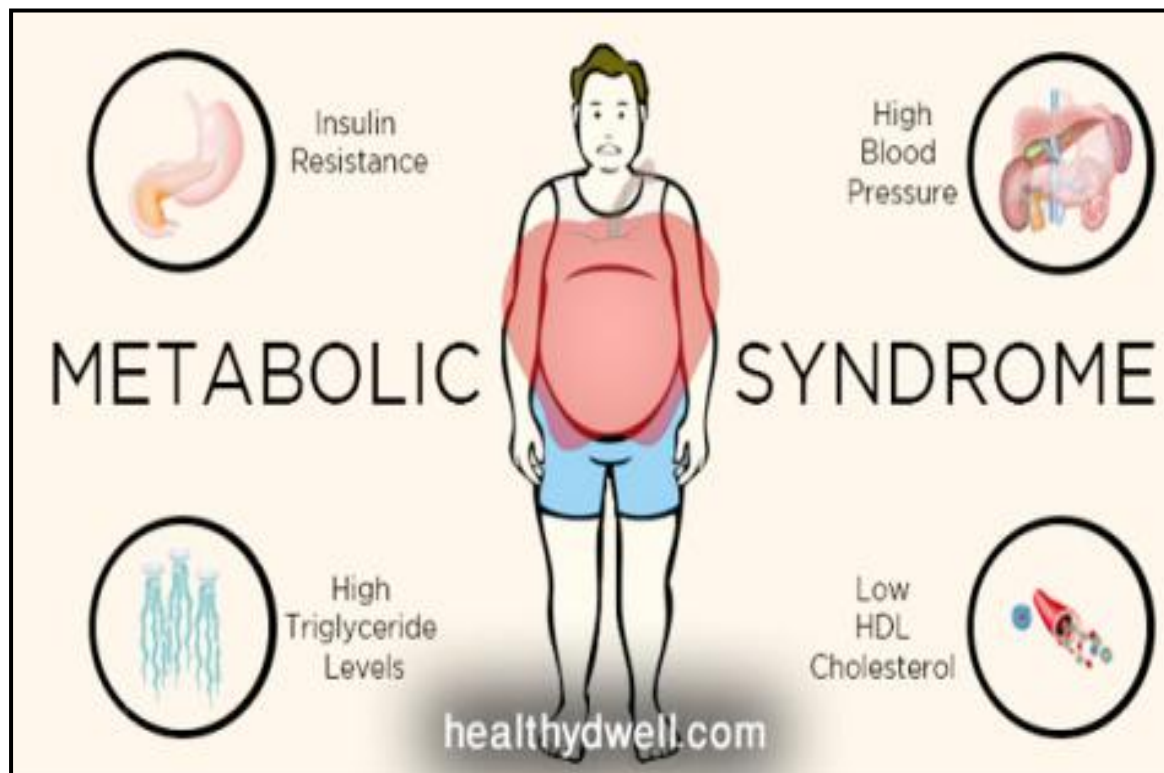
Metabolic syndrome

Definition

A cluster of metabolic abnormalities associated with abdominal obesity

(**Central obesity)**

Includes

- Hyperglycemia

- Insulin resistance

- Dyslipidemia: (Increased total cholesterol level and/or LDL-cholesterol and/or decreased HDL-cholesterol and/or increased triglycerides levels).

- Hypertension

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Which one of the following hormones increase insulin sensitivity?

A. Leptin

B. Adiponectin

C. Gherlin

D. CCK

Which one of the following hormones is hunger hormone?

A. Leptin

B. Adiponectin

C. Gherlin

D. CCK

Calculate:

Calculate the BMI for a patient ,the weight of this patient was 85.5 Kg and the height was 155 cm.

Answer:

1. Firstly convert the height to meters:

155 cm = 1.55 m

2. BMI = weight (kg)/height (m²) =
85.5/(1.55)² =35.6 kg/m².